AVROBIO

Cowen and Company 40th Annual Health Care Conference

March 2, 2020

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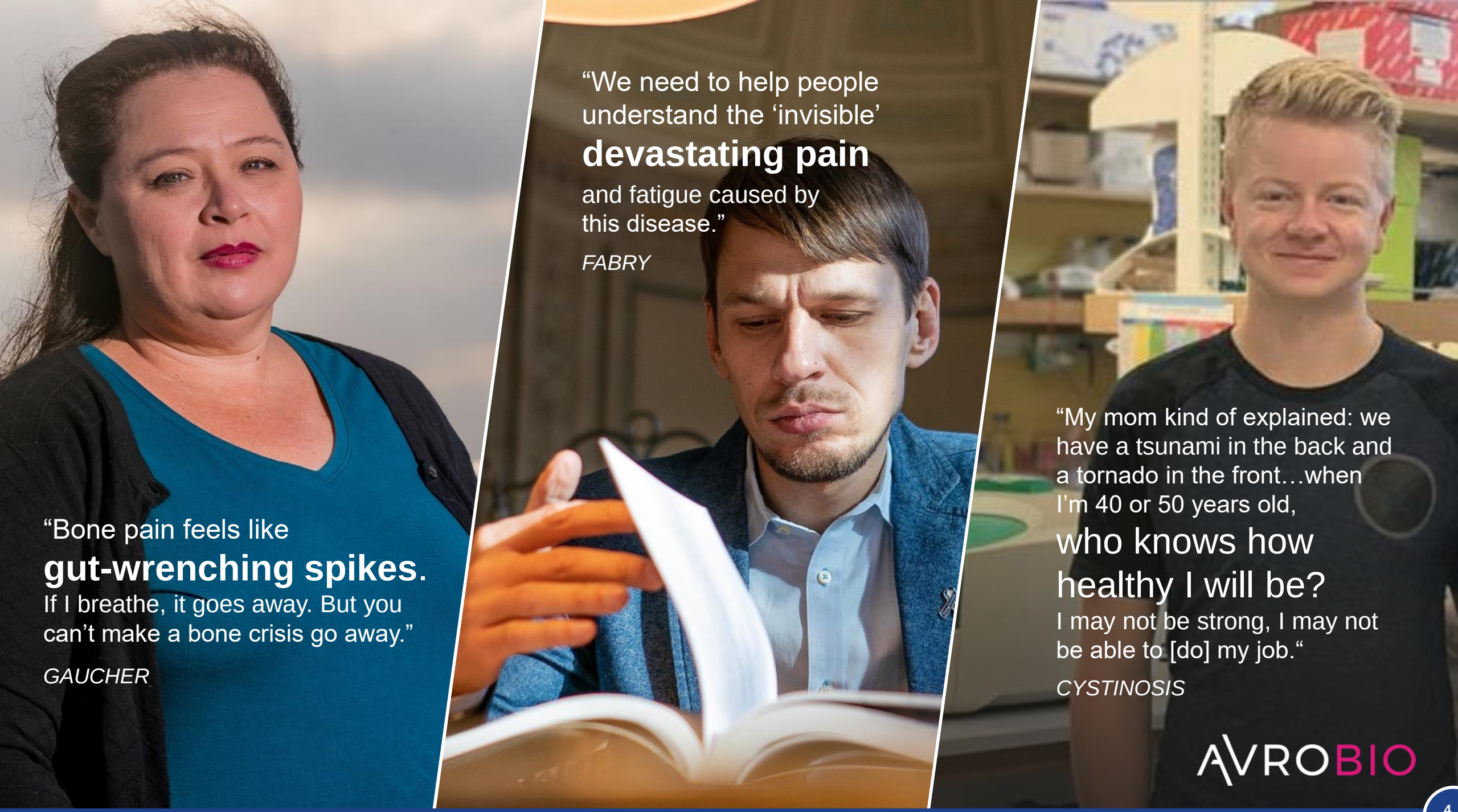
POWERED BY AVROBIO plato


AVROBIO
Our mission: Giving people with genetic disease freedom for life


“Bone pain feels like
gut-wrenching spikes.
If I breathe, it goes away. But you can’t make a bone crisis go away.”
GAUCHER
“We need to help people understand the ‘invisible’
devastating pain
and fatigue caused by this disease.”
FABRY
“My mom kind of explained: we have a tsunami in the back and a tornado in the front…when I’m 40 or 50 years old,
who knows how healthy I will be?
I may not be strong, I may not be able to [do] my job.“
CYSTINOSIS
AVROBIO

Building value across pipeline and platform

	2019 Accomplishments *…entered 2019 with one program in clinic*	2020 Accomplishments & Anticipated Milestones *generating data across 3 clinical programs in 2020…*
FABRY	✓ Reported additional data, including 87% substrate reduction in first kidney biopsy ✓ 9 patients dosed to date	✓ Additional patient data reported in February • Continue to report data during the year
GAUCHER	✓ Initiated patient recruitment	✓ First patient consented in Q1 2020 • Report initial patient data in 2H 2020
CYSTINOSIS	✓ First patient dosed	✓ Initial patient data reported in February • Continue to report data during the year
POMPE	✓ Initiated pre-clinical IND-enabling study	• Complete pre-clinical IND-enabling activities
AVROBIO	✓ Expanded management team ✓ Strengthened balance sheet with $138 million follow-on offering	✓ Strengthened balance sheet with $100 million follow-on offering; 2+ years cash runway • First AVROBIO “R&D Day” to be held this year
plato™	✓ Rolled out plato™ platform ✓ Dosed first patient under plato™ platform	✓ Initial plato™ data reported in February • Manufacture on 3 continents

IND: Investigational New Drug

POWERED BY AVROBIO plato™

Multiple programs in the clinic

10 patients dosed; 3 programs actively recruiting

Investigational Gene Therapy	Proof-of-Concept	IND-Enabling	Phase 1/2	Commercial Rights
Fabry AVR-RD-01	Phase 2			AVROBIO
Gaucher AVR-RD-02	Phase 1/2			AVROBIO
Cystinosis AVR-RD-04	Phase 1/2			AVROBIO
Pompe AVR-RD-03				AVROBIO

IND: Investigational New Drug

Addressing multi-billion dollar market opportunity

CURRENT STANDARD OF CARE COSTS

Disease	Est. Cost Per Patient Per Year	Approx. 2018 Net Sales	Selected Companies
Fabry	$320k	$1.4B	SANOFI GENZYME, Takeda Shire
Gaucher	$250k-400k	$1.4B	SANOFI GENZYME, Takeda Shire
Pompe	$500k	$1B	SANOFI GENZYME
Cystinosis	$625k-700k*	$0.2B	HORIZON PHARMA, Mylan, RECORDATI

Sources: Rombach S et al, Orphanet J Rare Dis, 2013; van Dussen L et al, Orphanet J Rare Dis, 2014; WAC pricing from Redbook; 2018 Net Sales from company annual and other reports
** for Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate)*
Note: Shire acquired by Takeda in 2019

Established *ex vivo* lentiviral approach

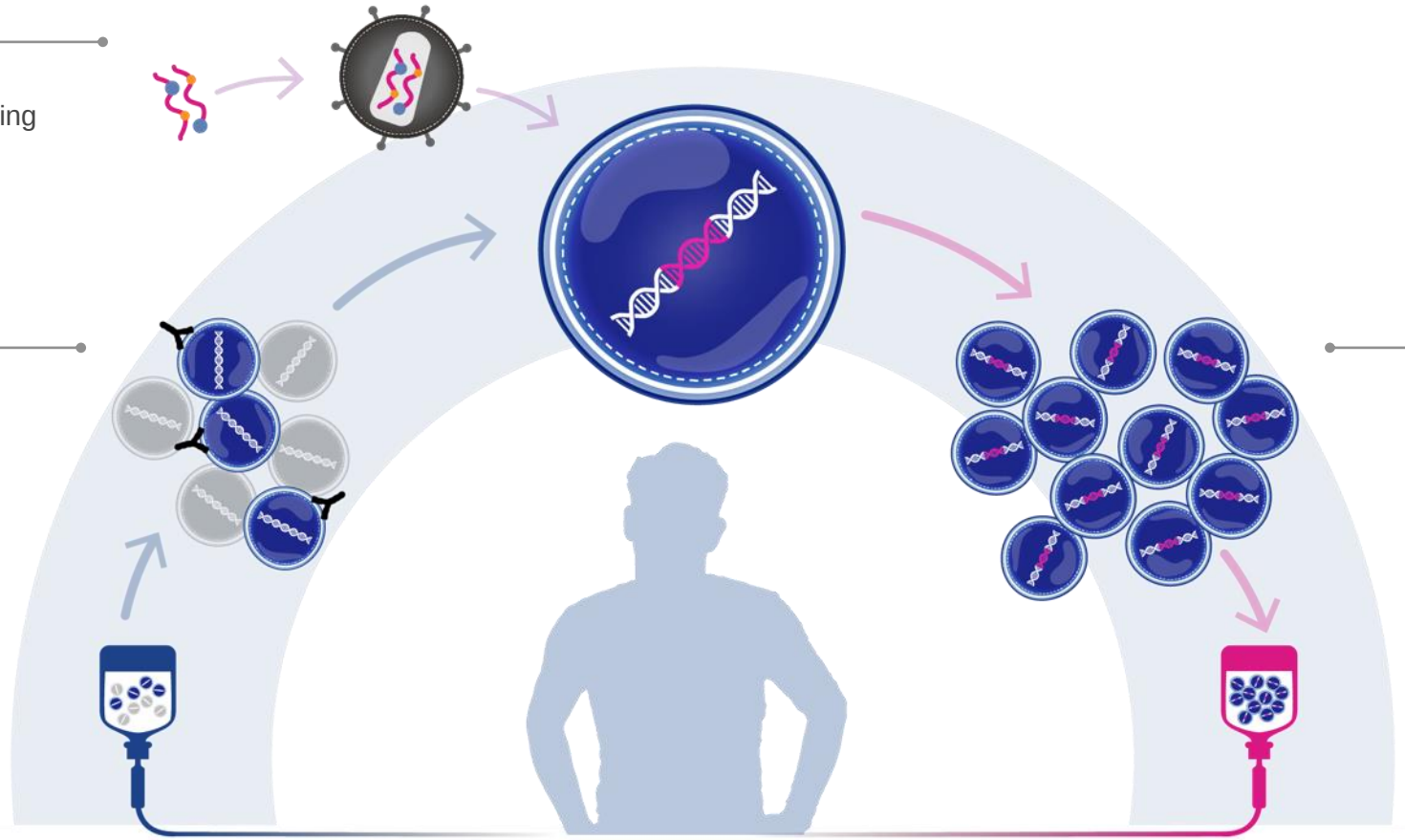
3 **Transduce** with lentiviral vector carrying normal gene

2 **Select** CD34+ stem cells

1 **Collect** mobilized blood

Harvest and freeze **4**

Infuse **5**



GENE THERAPY APPROACH

Fabry Disease

AVR-RD-01

Two AVR-RD-01 Fabry clinical trials

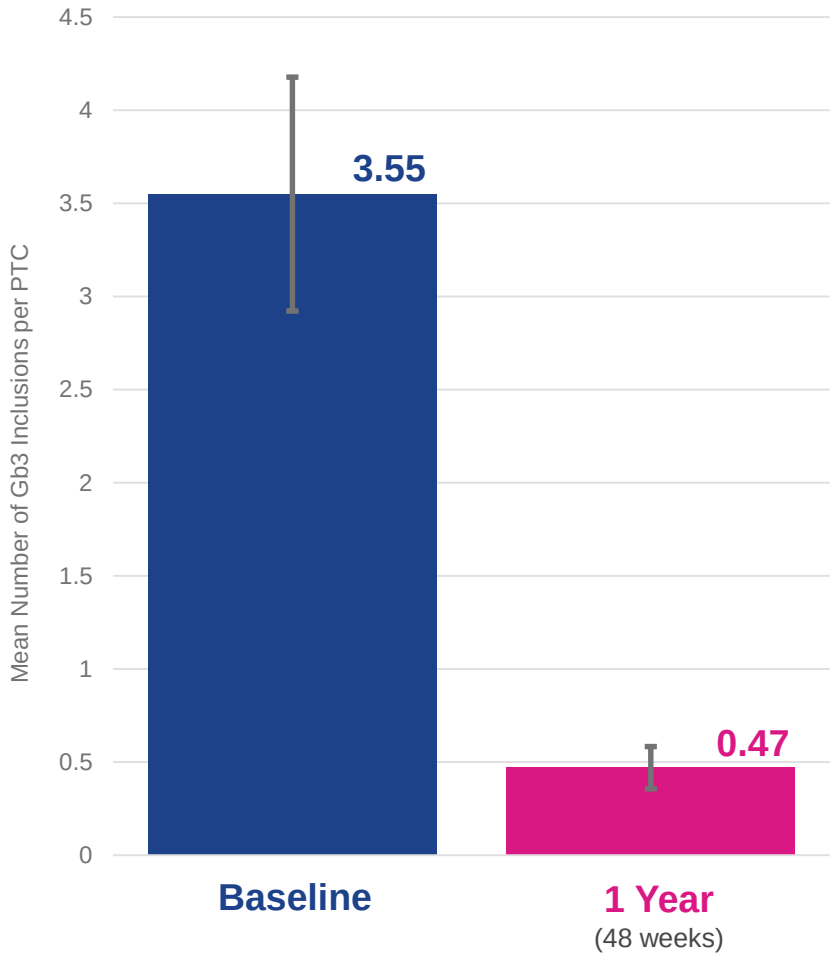
9 patients dosed across Phases 1 and 2

PHASE 1 Investigator-Sponsored Trial*	PHASE 2 AVRO – FAB-201 Trial
Patients **n = 5 (fully enrolled)** **On ERT > 6 months prior to enrollment** **18 - 50 year-old males**	**Patients** **n = 8-12 (4 patients dosed to-date)** **Treatment-naive** **16 - 50 year-old males**
Key Objective Safety and preliminary efficacy	**Key Objectives** Safety and efficacy

July 2019 data presented, unless otherwise specified
** Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada*

Patient 1: 87% substrate reduction in kidney biopsy at 1 year

Average number of **Gb3 inclusions per peritubular capillary (PTC)**

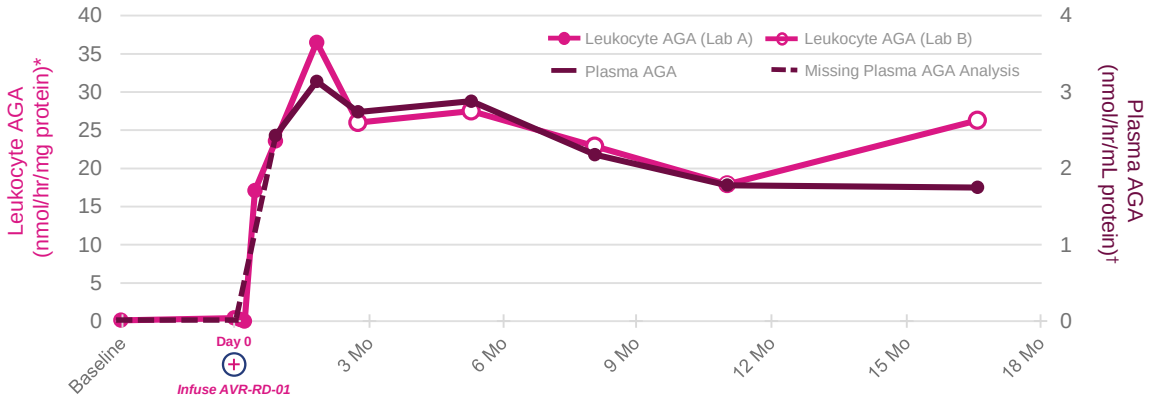


- *Unpaired t-test for difference between n=55 PTCs at baseline vs. n=101 PTCs at 1 year; p < 0.0001*
- *Error bar represents the standard deviation*

Baseline: The last available, non-missing observation prior to AVR-RD-01 infusion
Note: With respect to Fabry disease, Gb3 inclusions per PTC is interchangeable with GL-3 inclusions per KIC
FAB-201-1: First patient in FAB-201 clinical trial
PTC: Peritubular Capillary; Gb3: Globotriaosylceramide; GL-3: Globotriaosylceramide; KIC: Kidney Interstitial Capillary

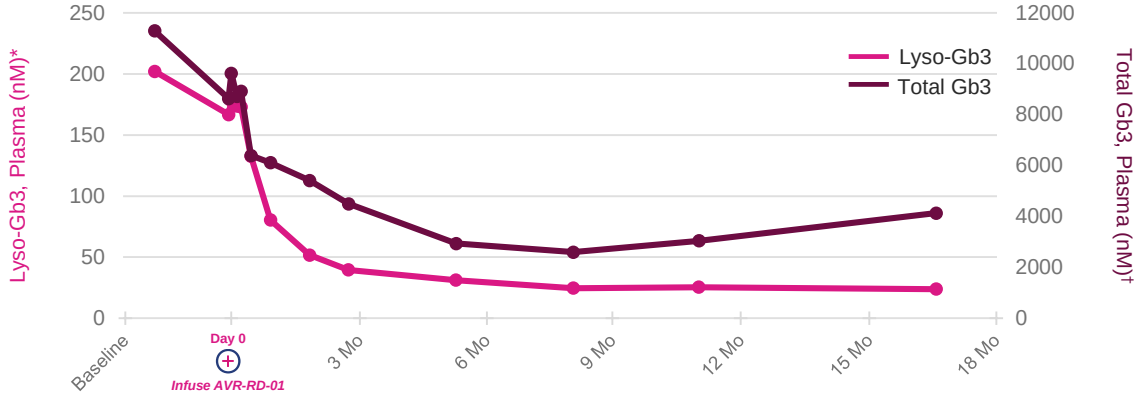
Patient 1: Multiple data trends sustained up to 18 months

Leukocyte + Plasma AGA Enzyme Activity



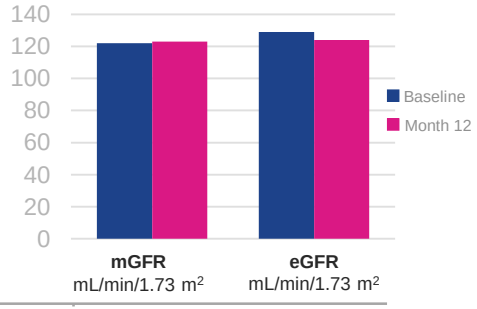
*Lab A: Mayo Clinic Laboratories; Lab B: Rupar Laboratory; Lab A Reference Range: >23.1 nmol/hr/mg; Lab B Reference Range: 24–56 nmol/hr/mg
†Reference Range: 5.1–9.2 nmol/hr/mL
AGA: α-galactosidase A

Plasma Lyso-Gb3 and Total Gb3



*Reference Value: 2.4 nM
†Reference Value: 4961 nM; 6012 nM before August 2018 (until Day 28 for Patient 1)
Lyso-Gb3: Globotriaosylsphingosine; Gb3: Globotriaosylceramide

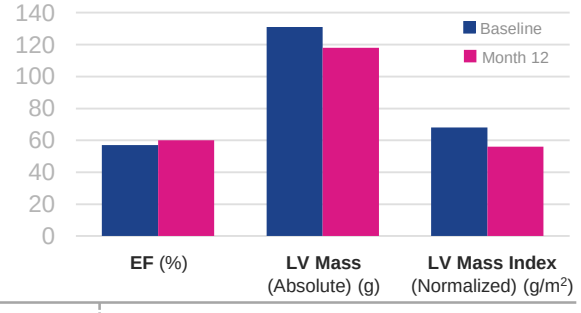
KIDNEY FUNCTION
remains within normal range at 12 mos.



Normal Range mGFR/eGFR	Average 116* mL/min/1.73 m² *Male (20–39 years)*	

*Source: https://www.kidney.org/atoz/content/gfr
mGFR: Measured Glomerular Filtration Rate; eGFR: Estimated Glomerular Filtration Rate

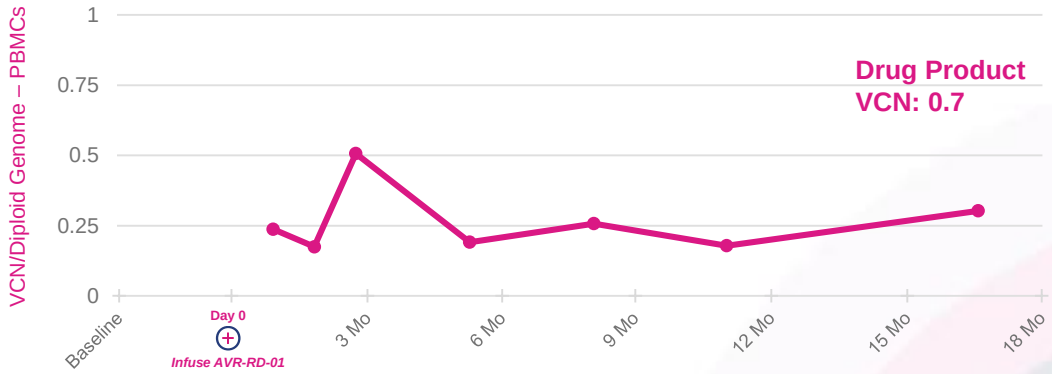
CARDIAC FUNCTION
remains within normal range at 12 mos.



Reference Range Mean Values ± SD	64.3 ± 4.2%	138.9 ± 24.5 g *Male (20–39 years)*	67.8 ± 10.7 g/m²

Source: *Alfakih K et al, J Magn Reson Imaging, 2003*
EF: Ejection Fraction; LV: Left Ventricular

Vector Copy Number (VCN)

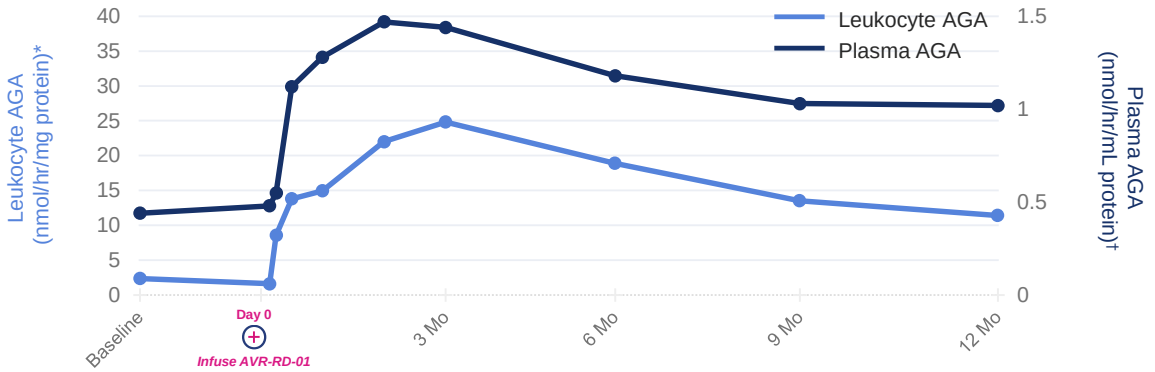


VCN: Vector Copy Number; PBMCs: Peripheral Blood Mononuclear Cells

Note: Patient #1 had a skin biopsy score of 3 (severe accumulation) at baseline, a score of 2 (moderate accumulation) at 6 months and a score of 1 (mild accumulation) at 12 months

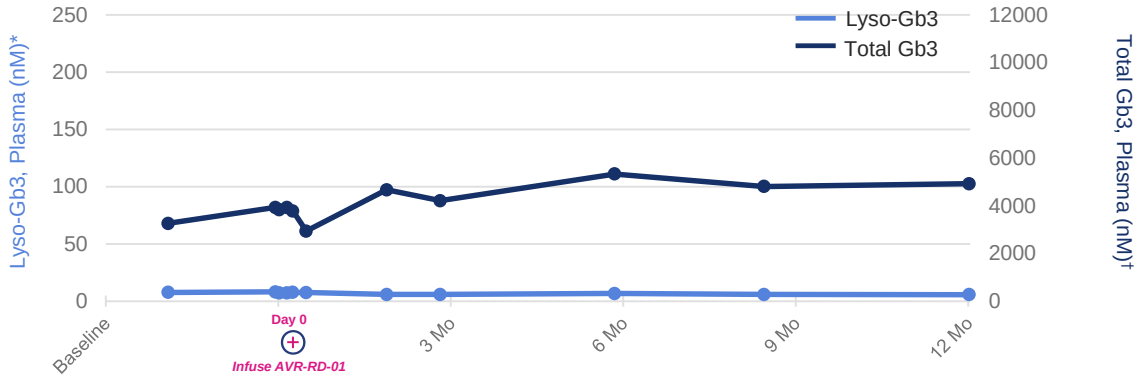
Patient 2: Multiple data trends sustained up to 12 months

Leukocyte + Plasma AGA Enzyme Activity



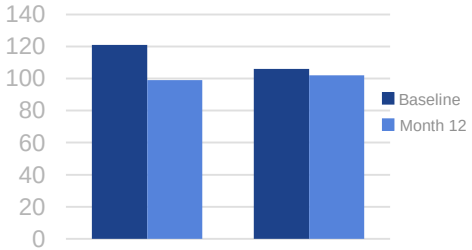
*Data from Rupar Laboratory; Reference Range: 24–56 nmol/hr/mg
†Reference Range: 5.1–9.2 nmol/hr/mL
AGA: α-galactosidase A

Plasma Lyso-Gb3 and Total Gb3



*Reference Value: 2.4 nM; †Reference Value: 4961 nM
Note: Patient #2 has normal substrate, consistent with late-onset cardiac variant phenotype
Lyso-Gb3: Globotriaosylsphingosine; Gb3: Globotriaosylceramide

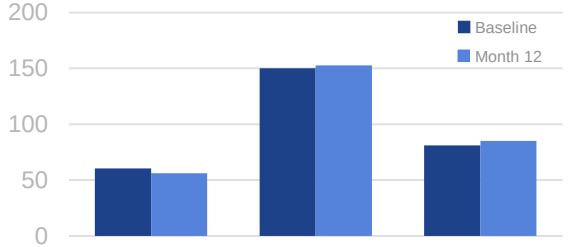
KIDNEY FUNCTION *remains within normal range*



Normal Range mGFR/eGFR	Average 99 mL/min/1.73 m² *Male (40–49 years)*

Source: https://www.kidney.org/atoz/content/gfr
mGFR: Measured Glomerular Filtration Rate; eGFR: Estimated Glomerular Filtration Rate

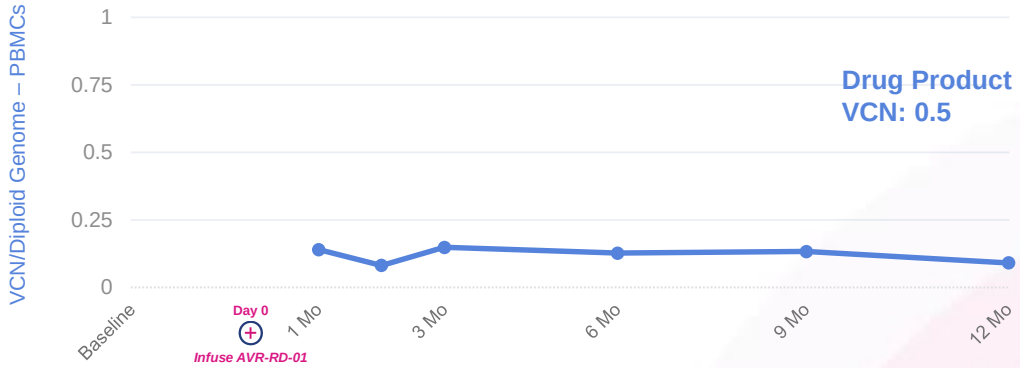
CARDIAC FUNCTION *remains within normal range*



Reference Range Mean Values Male 40-49 years	55–65%	58–91 g/m²

Source: Alfakih K et al, J Magn Reson Imaging, 2003
EF: Ejection Fraction; LV: Left Ventricular

Vector Copy Number (VCN)

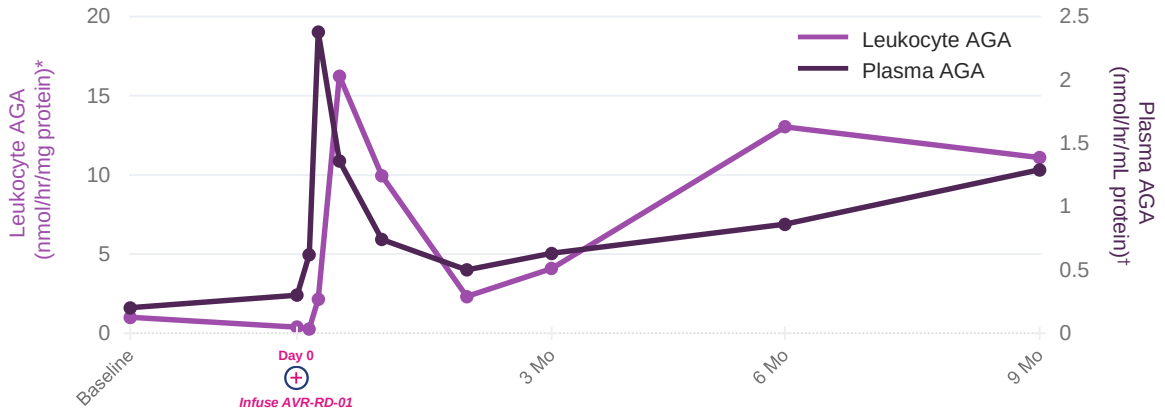


VCN: Vector Copy Number; PBMCs: Peripheral Blood Mononuclear Cells

Note: As patient #2 is a cardiac variant of Fabry disease, this patient had a skin biopsy score of 0 (trace or no accumulation) at baseline and at 6 months

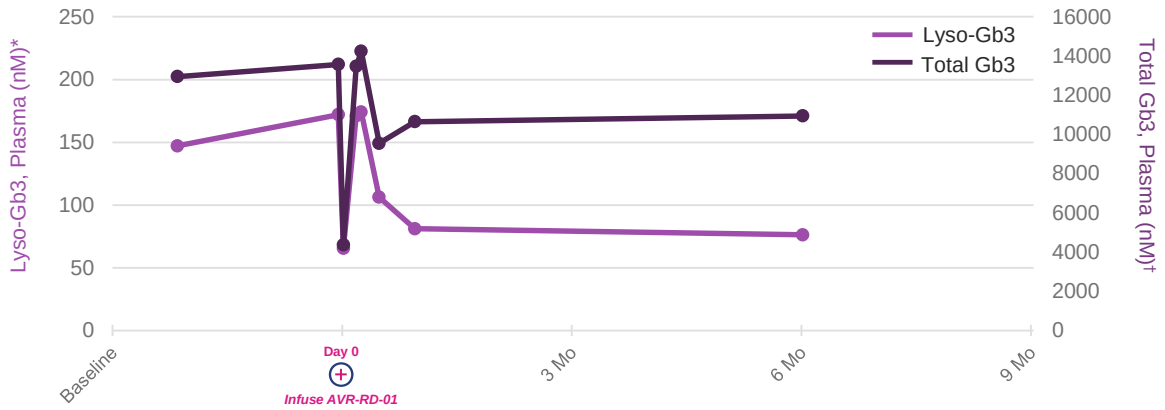
Patient 3: Initial divergent profile with 9 month data trending toward anticipated long-term engraftment

Leukocyte + Plasma AGA Enzyme Activity



*Data from Rupar Laboratory; Reference Range: 24–56 nmol/hr/mg
†Reference Range: 5.1–9.2 nmol/hr/mL
AGA: α-galactosidase A

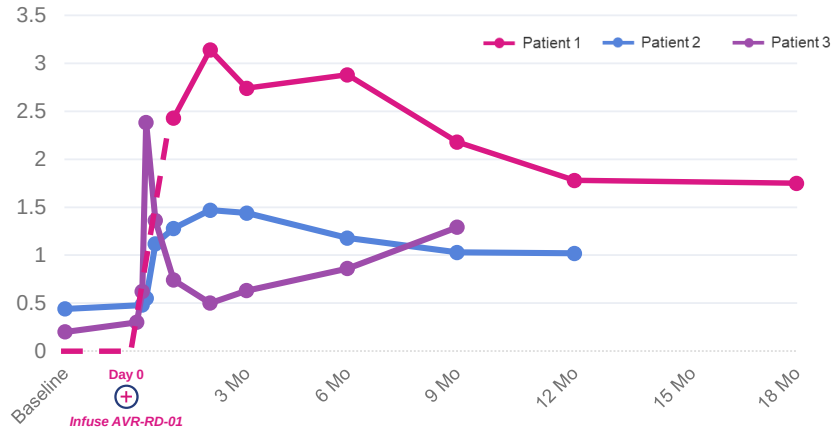
Plasma Lyso-Gb3 and Total Gb3



*Reference Value: 2.4 nM
†Reference Value: 4961 nM
Lyso-Gb3: Globotriaosylsphingosine; Gb3: Globotriaosylceramide

Skin Biopsy Score (Patient 3)	
Baseline	2
6 months	2

Plasma AGA Enzyme Activity



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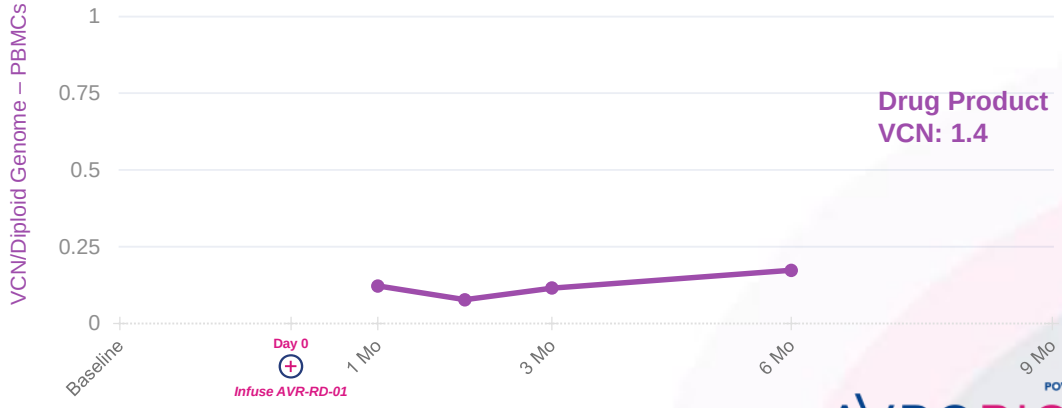


VCN: Vector Copy Number; PBMCs: Peripheral Blood Mononuclear Cells

Two AVR-RD-01 Fabry clinical trials

9 patients dosed across Phases 1 and 2

PHASE 1
Investigator-Sponsored Trial*

Patients

n = 5 (fully enrolled)
On ERT > 6 months prior to enrollment
18 - 50 year-old males

Key Objectives

Safety and preliminary efficacy

PHASE 2
AVRO – FAB-201 Trial

Patients

n = 8-12 (4 patients dosed to-date}
Treatment-naive
16 - 50 year-old males

Actively enrolling

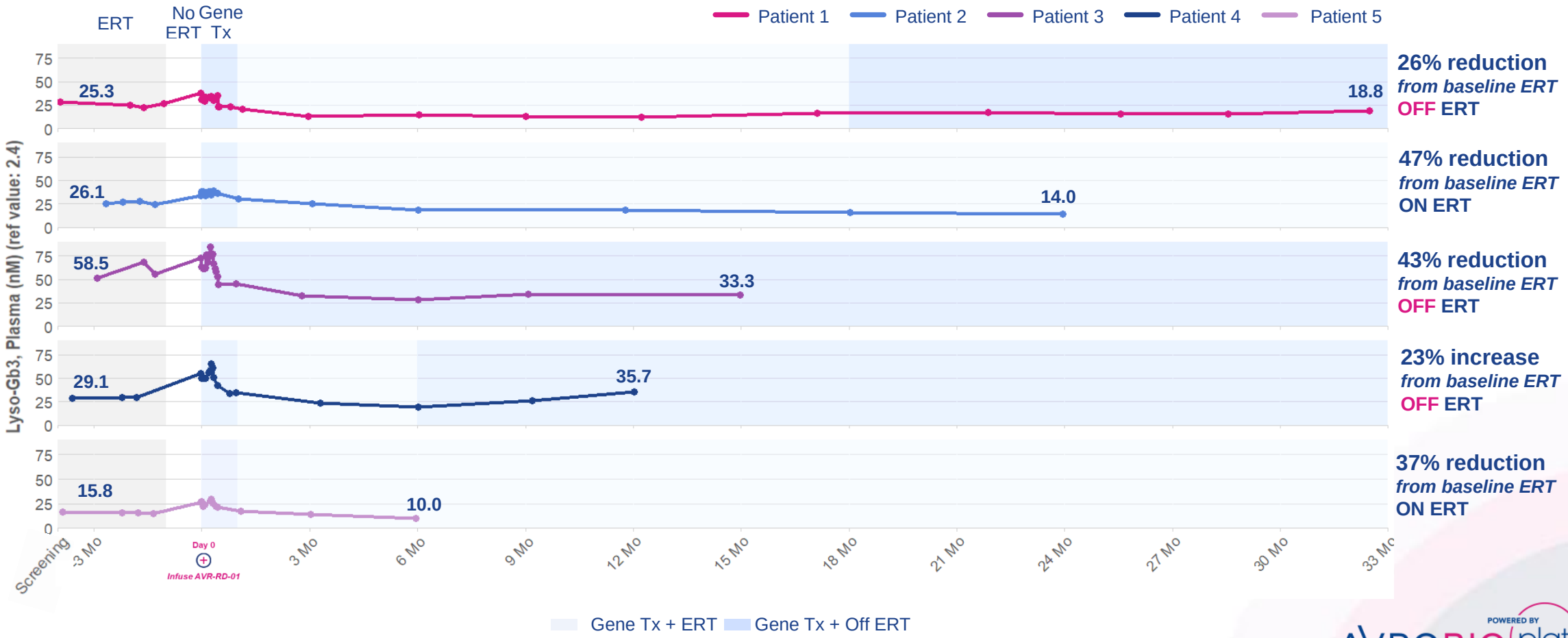
Key Objectives

Safety and efficacy

FAB-201 = AVRO-RD-01-201 Study
** Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada*
ERT: Enzyme Replacement Therapy

Patients 1-5: Plasma lyso-Gb3 reduction sustained up to 32 months

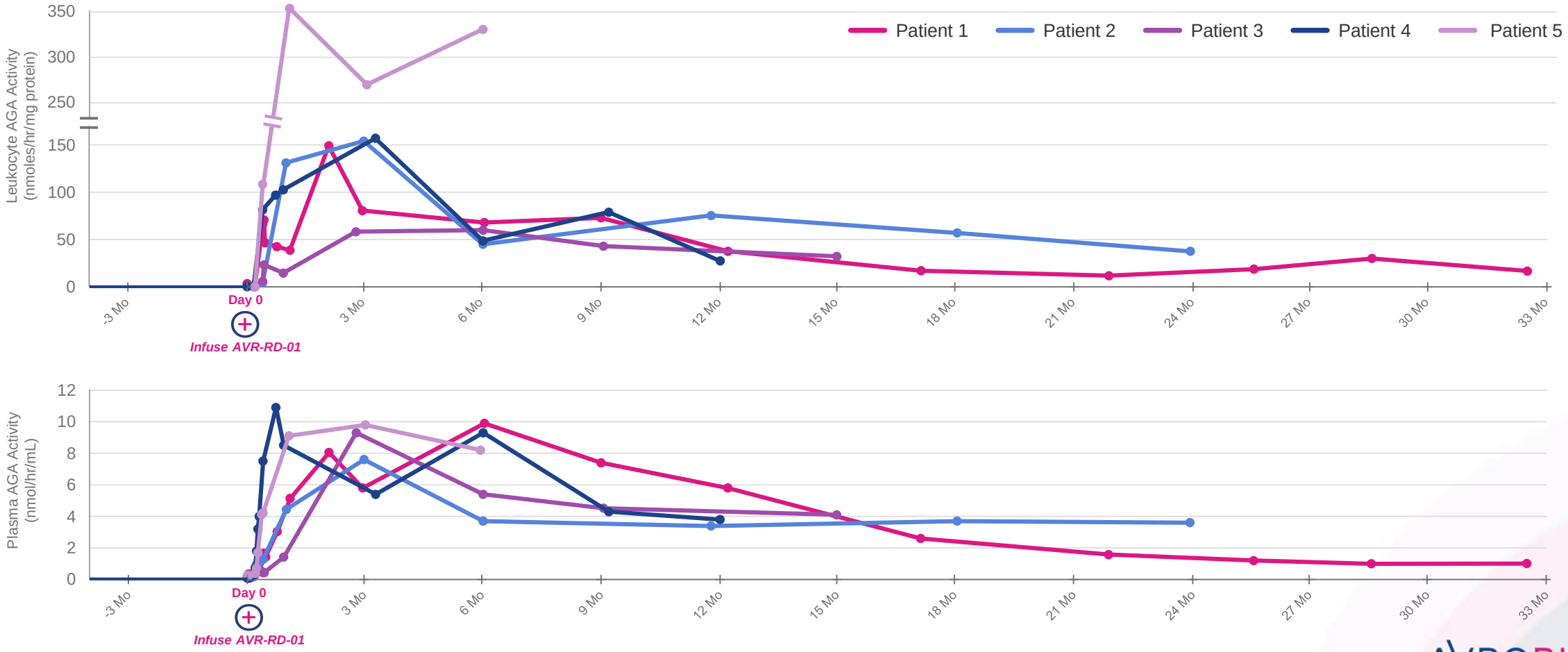
All patients who have discontinued ERT remain off ERT



Lyso-Gb3: Globotriaosylsphingosine; ERT: Enzyme Replacement Therapy; Tx: Therapy

Patients 1-5: Leukocyte and plasma enzyme activity sustained up to 32 months

Consistent trends across all patients, 4 patients > 1 year

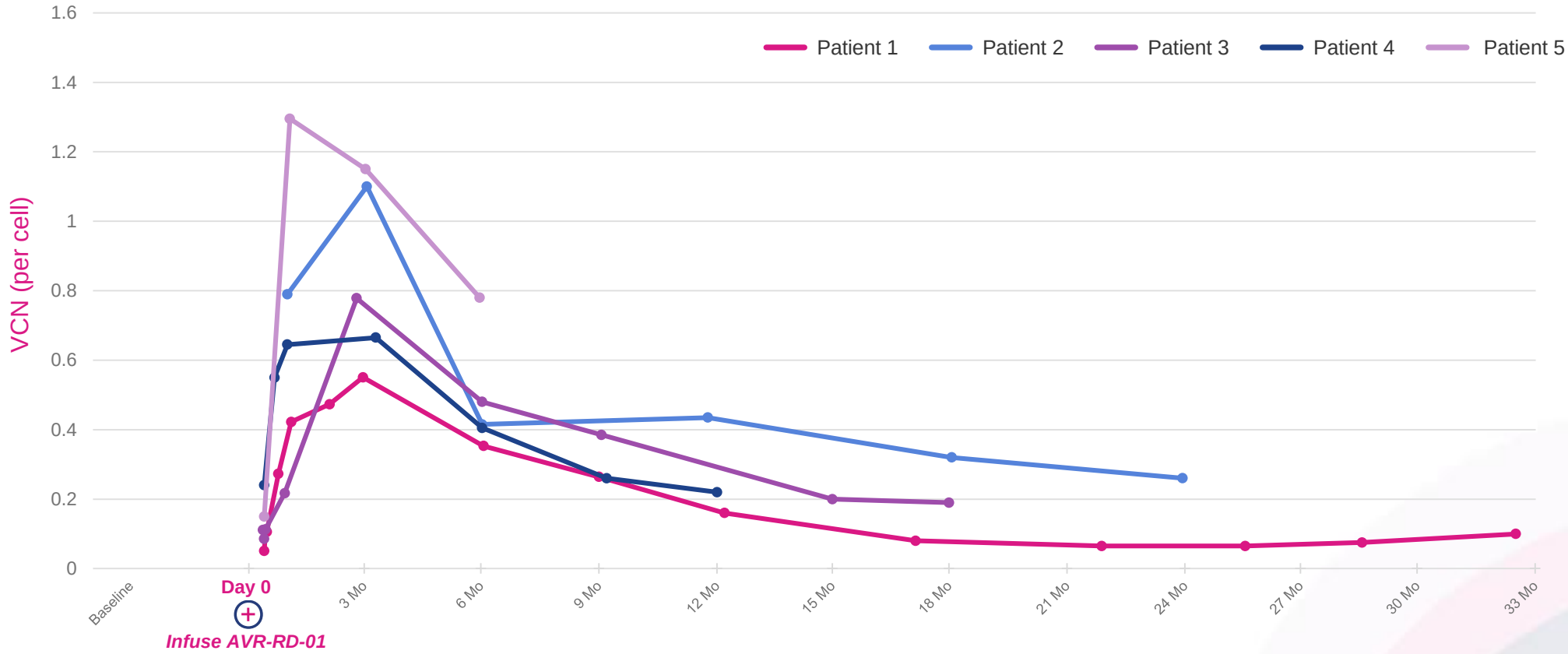


AGA: α-Galactosidase A

VCN stable at 32 months with consistent trend across all other patients

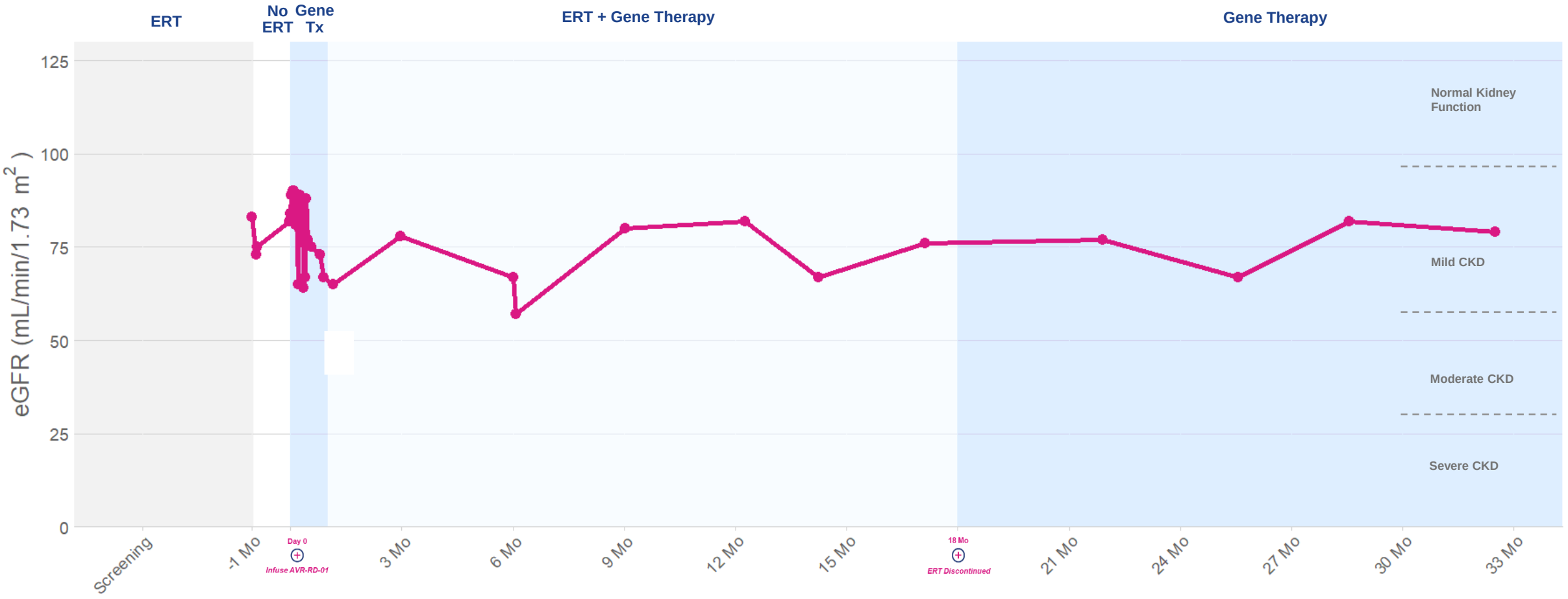
4 patients with 1+ years data

Drug Product VCN	
Patient 1	0.7
Patient 2	1.4
Patient 3	0.8
Patient 4	1.4
Patient 5	1.2



Note: 0.1 VCN is indicative of approx. 5-10% of all nucleated cells having an average of 1-2 copies of the transgene
VCN: Vector Copy Number

Patient 1: Kidney function stable at 32 months



eGFR: Estimated Glomerular Filtration Rate; ERT: Enzyme Replacement Therapy; TX: Therapy; CKD: Chronic Kidney Disease

Phase 1 Fabry (5 patients) and FAB-201 (4 patients)

No unexpected safety events or trends identified

No SAEs related to AVR-RD-01 drug product

AEs and SAEs reported

Phase 1 AEs (n = 128):

- Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions

Phase 1SAEs (n = 2):

- Febrile neutropenia (grade 3)
- Thrombophlebitis (grade 2)

FAB 201 AEs (n = 98):

- Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
  - Grade 1 or 2 (n = 72)
  - Grade 3 or 4 (n = 30)

FAB 201 SAEs: (n = 4)

Pre-treatment and prior to conditioning

- Seizure (grade 2)

Post-treatment

- Dehydration, nausea, vomiting (grade 3)
- Febrile neutropenia (2 patients, grade 3 & 4)

Anti-AGA antibodies

- Pre-existing low titers detected in 4 patients

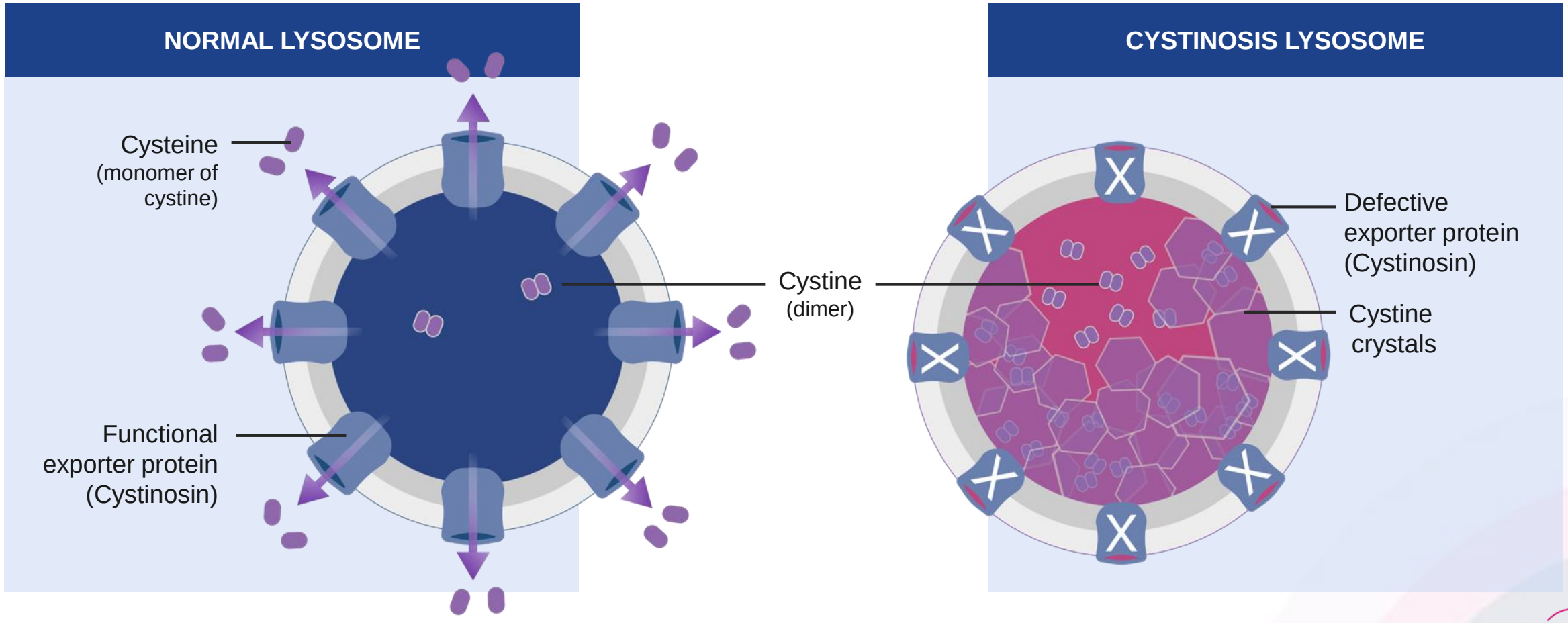
Note: Safety data cut November 26, 2019
AE: Adverse Event; SAE: Serious Adverse Event
NOTE: AVR-RD-01 is an investigational gene therapy

Cystinosis

AVR-RD-04

Cystinosis caused by defective gene that encodes cystinosin, an exporter protein

Cystine crystals build up in lysosomes causing tissue and organ damage



Source: Cherqui et al, Nat Rev Nephrol. 2017

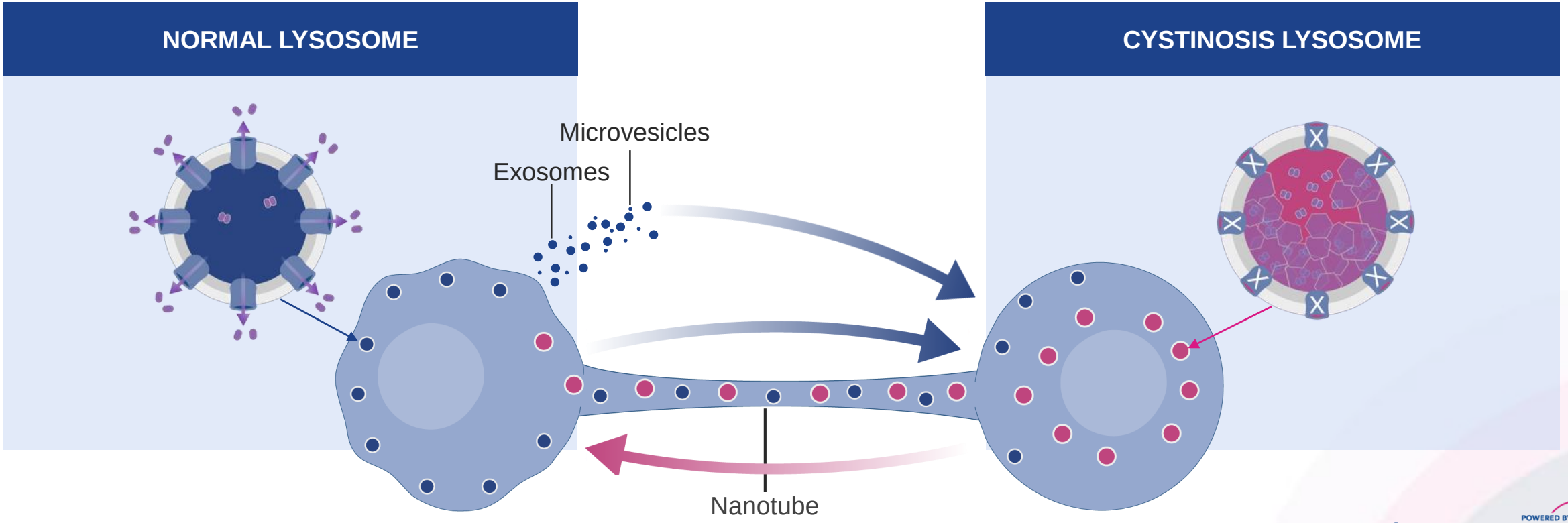
Drug product-derived macrophages restore normal cystine recycling

Mechanisms of action

Macrophages with CTNS transgene restore cystine recycling to CTNS^{-ve} cells via:

1. Tunneling nanotubes – transfer of corrected lysosomes, cystinosin, CTNS mRNA
2. Exosomes / Microvesicles – transfer of cystinosin, CTNS mRNA

Net result: Corrected lysosomes in cells throughout the body



Sources: Naphade, Stem Cells, 2015. Harrison, Molecular Therapy, 2013.
CTNS: cystinosin, lysosomal cystine transporter; mRNA: Messenger Ribonucleic Acid

Investigator-sponsored* study of AVR-RD-04 in cystinosis patients

First patient dosed

PHASE 1/2
Investigator-Sponsored Trial*

Patients

Up to 6 patients
Adults and adolescents
Cohorts 1-2 ≥18 years; Cohort 3 ≥14 years
Male and Female
On oral and ophthalmic cysteamine

Actively recruiting

Key Objectives

Safety and efficacy

** Sponsored by University of California, San Diego*
Note: AVR-RD-04 aka CTNS-RD-04

Phase 1/2 Cystinosis
1 patient dosed

No unexpected safety events or trends identified

No AEs or SAEs related to AVR-RD-04 drug product

No SAEs reported

AEs reported

- Consistent with myeloablative conditioning and underlying disease
- N = 22 (moderate = 9, mild = 13)

Pre-treatment and prior to conditioning (n = 6, not all events listed)

- Diarrhea, hypokalemia, dizziness
- Dehydration, vomiting

Post-treatment (n = 16, not all events listed)

- Alopecia, intermittent diarrhea, vomiting
- Mucositis, intermittent febrile neutropenia, intermittent epistaxis
- Intermittent blurry vision, intermittent hypokalemia, mucoceles
- Thrombocytopenia

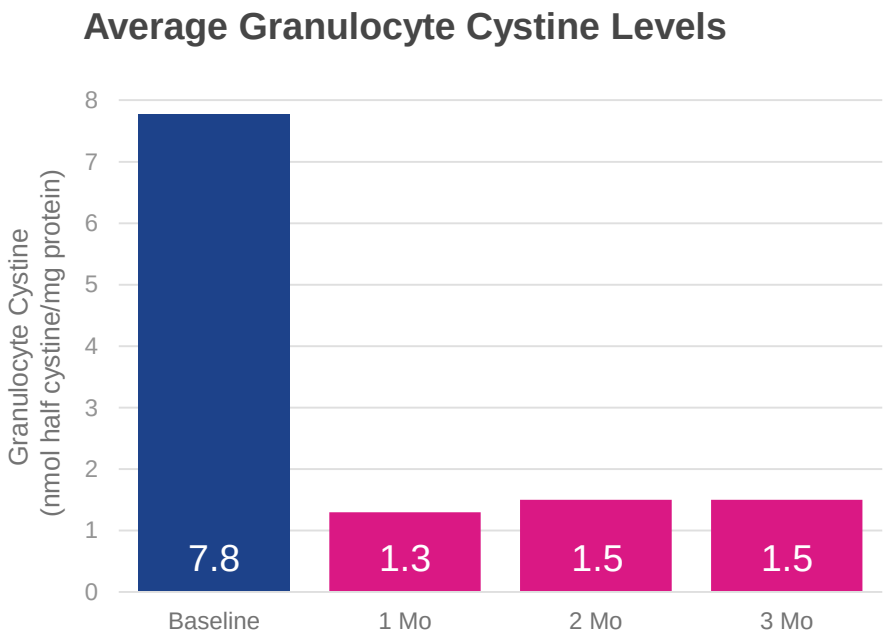
Note: Safety database cut as of January 27, 2020
AE: Adverse Event; SAE: Serious Adverse Event

Patient 1: Initial data suggest positive trends across multiple measures

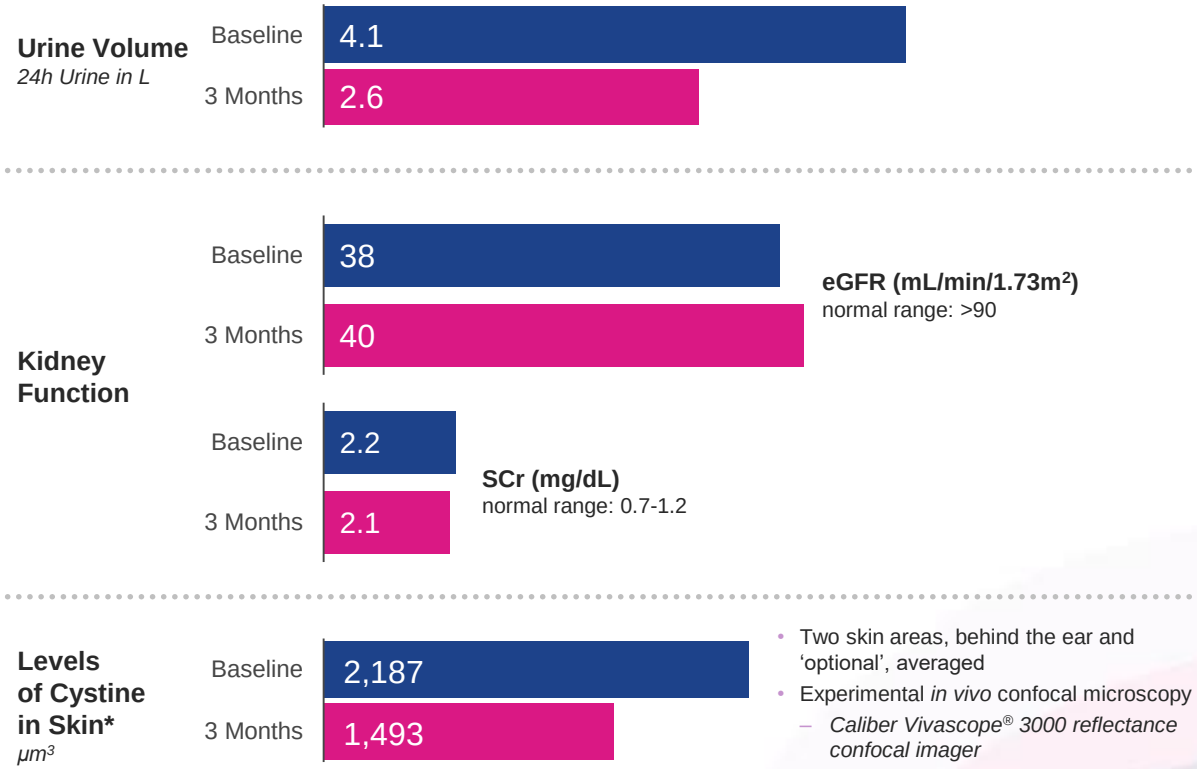
PRIMARY EFFICACY ENDPOINT

VCN
(Drug Product = 2.1)

1 month	2.9
2 months	3.0
3 months	2.0



SECONDARY ENDPOINTS



- Two skin areas, behind the ear and 'optional', averaged
- Experimental *in vivo* confocal microscopy
  - *Caliber Vivascope® 3000 reflectance confocal imager*
  - *Adapted for skin imaging; papillary dermis 16–40 µm*
- Analysis and quantification
  – 3D Image-Pro software

Asymptomatic Heterozygous Carrier Granulocyte Cystine Range: 0.2 – 1 .9 nmol half cystine/mg protein
Source: Gertsman I et al., Clinical Chemistry, 2016
VCN: Vector Copy Number; CTNS: Cystinosin, Lysosomal Cystine Transporter; mRNA: Messenger Ribonucleic Acid; eGFR: Estimated Glomerular Filtration Rate; SCr: Serum Creatinine
**Data obtained using a novel experimental methodology utilizing optical coherence tomography, to image crystals in the skin behind the ear*

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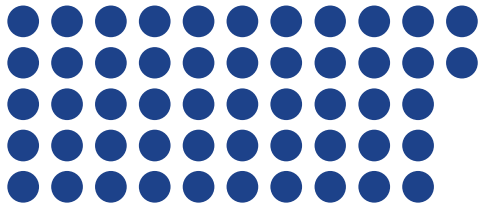
Patient 1: Reduced treatment burden at 3 months

Number of Medications and Supplements

(max per day)

Before Gene Therapy

ON Cysteamine

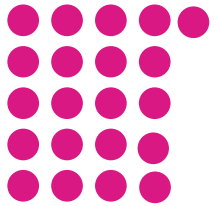


52

After Gene Therapy

(at 3 months post-gene therapy)

OFF Cysteamine



21

NOTE: Investigational gene therapy

Gaucher Disease

AVR-RD-02

Goals for gene therapy in **Gaucher Type 1 Disease**

UNMET NEEDS:

Bone-related manifestations
Unmet needs: bone pain, avascular necrosis, bone crisis, osteoporosis, fractures, joint destruction, skeletal abnormalities

Hemoglobin levels and platelet counts
Unmet needs: anemia, thrombocytopenia, easy bruising, bleeding

Hepatosplenomegaly
Unmet needs: enlarged liver, enlarged spleen

CNS complications
Unmet needs: Increased risk of GBA-Parkinson's disease

Everyday burden of illness, and life expectancy
Unmet needs: fatigue, pain, lung disease, biweekly infusions, shortened lifespan

Sources: Grabowski G et al, Online Metabolic and Molecular Bases of Inherited Disease, 2018; Weinreb N et al, AJH, 2008; Pastores G et al, Semin Hematol, 2004
CNS: Central Nervous System; GBA: gene coding for glucocerebrosidase

Long-term follow-up study highlights significant unmet need in Gaucher Type 1

Despite standard-of-care ERT, **disease progression** continues and **unmet need** remains.

Incomplete therapeutic response is common:

- **60%** of patients failed to achieve at least one of the six therapeutic goals evaluated after 4+ years of ERT[1]
- A clinically significant percentage of patients continue to exhibit **bone pain, organomegaly and cytopenia** after 10 years of ERT[2]
- **25%** of patients continue to suffer from physical limitations after two years of ERT, primarily due to bone disease[3]

Persistence after **10 years ERT†**	**Non-splenectomized** Patients	**Splenectomized** Patients
Anemia	12.4%	8.8%
Thrombocytopenia*	22.7%	0.7%
Splenomegaly*	38.3%	N/A
Hepatomegaly*	14.3%	18.8%
Bone Pain	42.9%	62.5%
Bone Crisis	7.4%	16.7%

* Higher persistence rates observed when more severe manifestations were present at baseline

† Persistence refers to the presence of anemia, bone pain, bone crisis, or at least moderate thrombocytopenia, splenomegaly, or hepatomegaly, present after 10 years of ERT among those with baseline involvement of these parameters (from a registry of 757 GD1 patients; Weinreb et al., 2013).

Following 10 years of treatment, ~26% of patients were receiving between 45-150 U/kg EOW, and 96% of these individuals were receiving doses between 45-90 U/kg EOW.

Sources: *[1]Weinreb N et al. Amer J Hematol, 2008; [2]Weinreb N et al. J Inherit Metab Dis, 2013; [3]Giraldo P et al. Qual Life Res, 2005.*

GD1: Gaucher Disease Type 1; SOC: Standard of Care; ERT: Enzyme Replacement Therapy; EOW: Every Other Week

Pompe disease

AVR-RD-03

Pompe preclinical program advancing

Integrated three-part approach

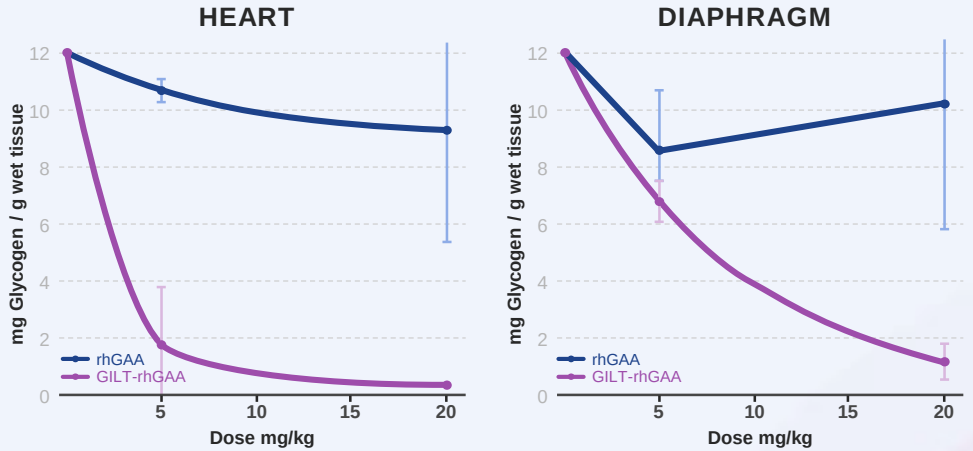
THE CHALLENGE

- Pompe requires **20x more ERT** than Fabry or Gaucher
- Requires GAA activity restored to **muscle and CNS**

AVROBIO's APPROACH

1. Potent transgene promoter
2. GILT uptake tag
3. plato™ for CNS impact

GILT-tagged Recombinant Human (rh)GAA impacts levels of stored glycogen compared to non GILT-tagged Recombinant Human (rh)GAA in a Pompe mouse model



GILT: Glycosylation-Independent Lysosomal Targeting
Sources: Burton B et al, J Pediatr, 2017; Ausems M et al, Eur J Hum Genet, 1999; Gungor D et al, Orphanet J Rare Dis, 2011; Maga JA et al, J of Bio Chem, 2013

plato™

AVROBIO's foundation designed to scale gene therapy worldwide

State-of-the-art technologies including automated manufacturing platform

- **Optimized** for performance
- **Redefines** manufacturing best practices

POWERED BY AVROBIO plato™

plato™: Three upgrades designed to optimize potency, safety and durability

UPGRADES	Increase enzyme activity	Increase transduction efficiency	Increase VCN	Increase marrow space / engraftment	Increase consistency and safety
1 | Vector	⊕	⊕	⊕		
2 | Conditioning			⊕	⊕	⊕ *
3 | Automation	⊕				⊕

Upgrades designed to increase Vector Copy Number (VCN), enzyme activity, chimerism and durability

* TDM (therapeutic drug monitoring)

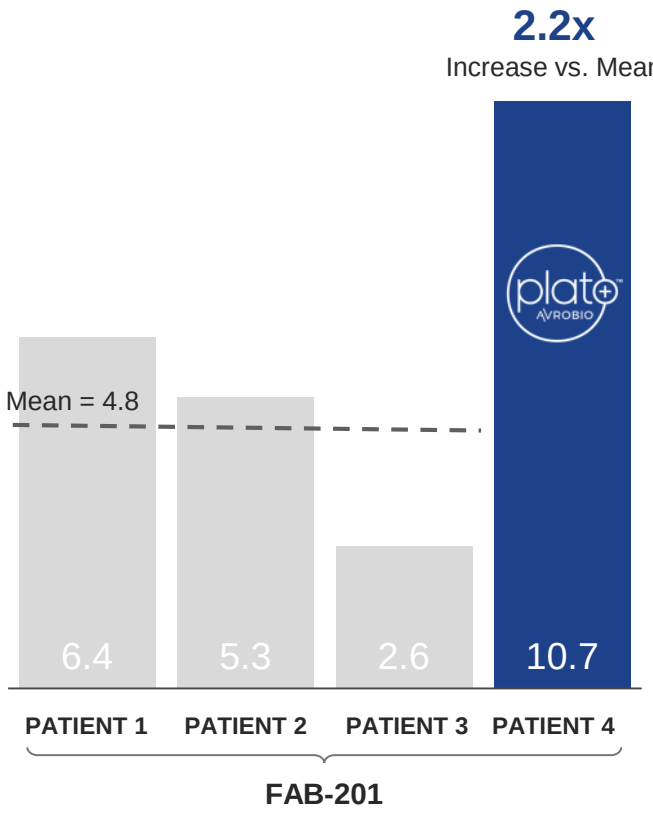
plato™ UPGRADE 1

VECTOR UPGRADE:

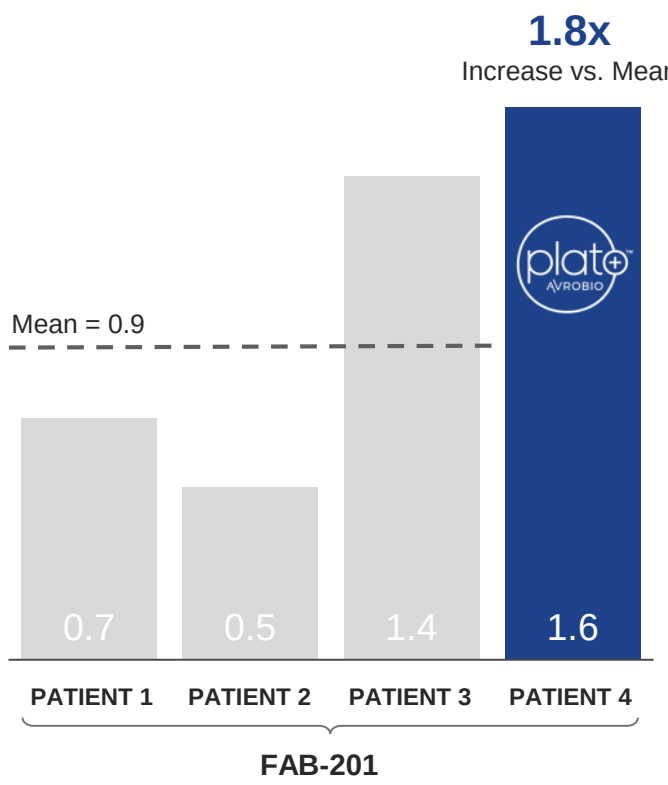
Metrics compared to academic process

FAB-201 patient #4 drug product data with plato™

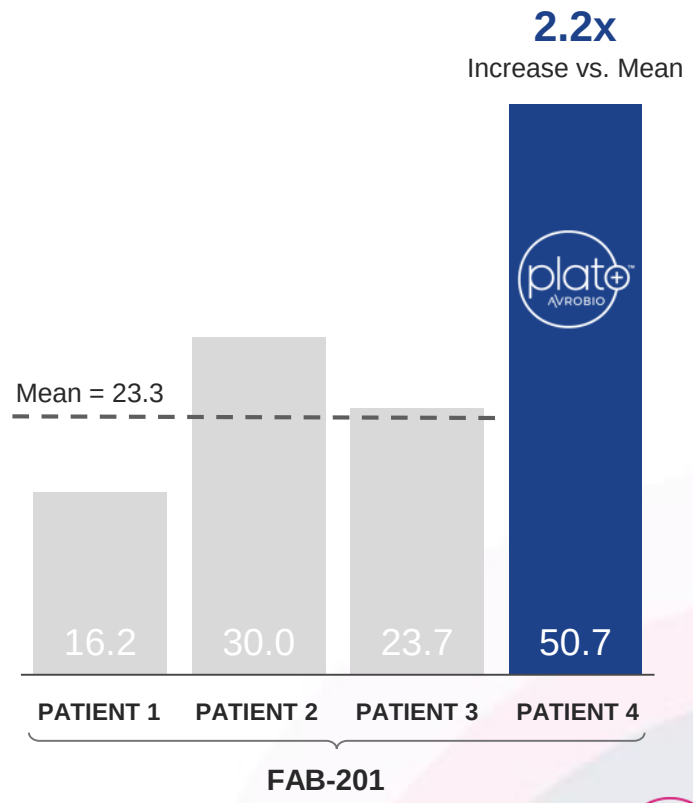
Enzyme Activity (nmol/hr/mL)



VCN (per diploid genome)



Transduction Efficiency (%)



VCN: Vector Copy Number; FAB-201: AVR-RD-01 Study
NOTE: Data is from drug product

POWERED BY AVROBIO plato™

plato™ UPGRADE 2

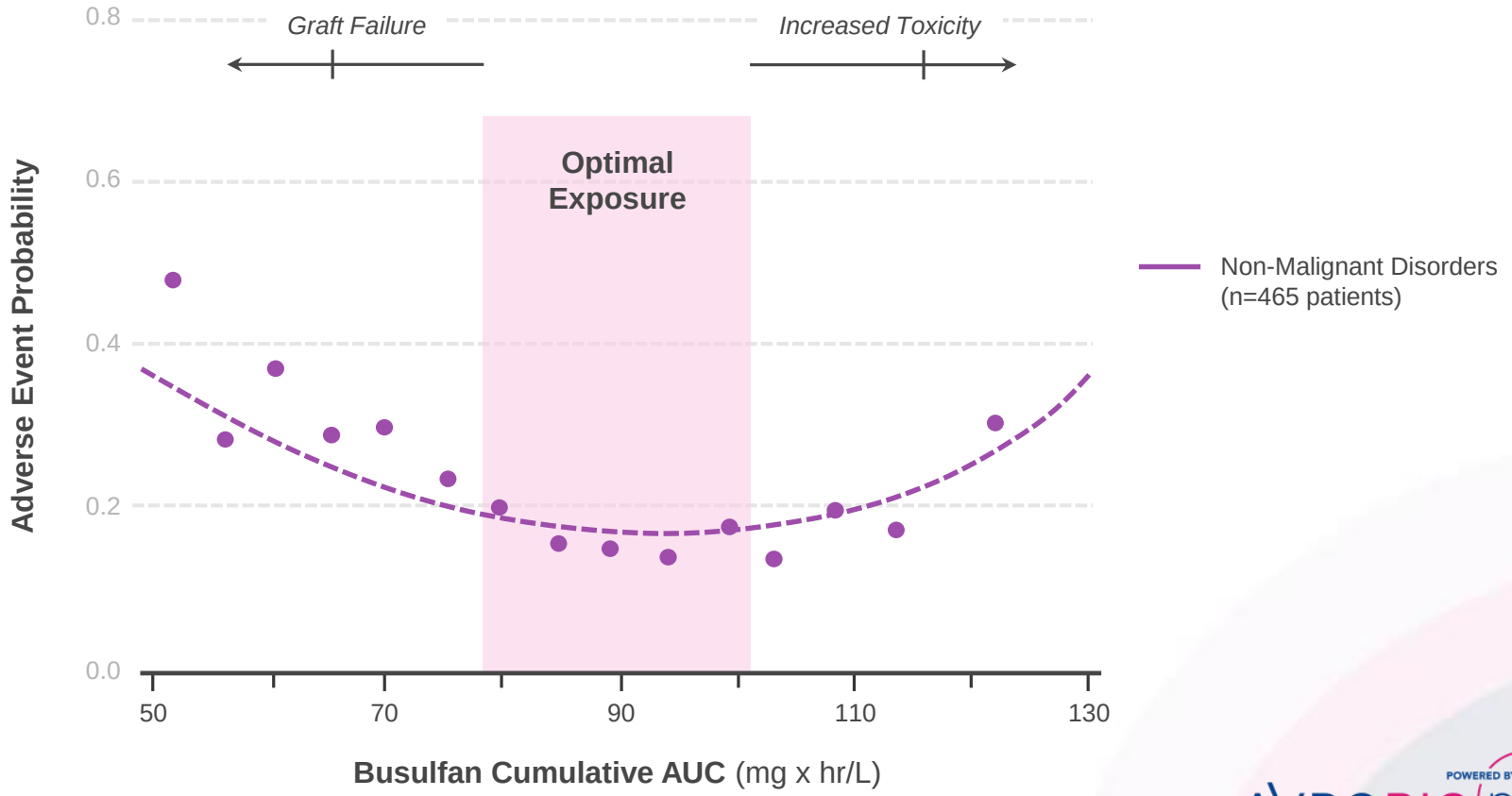
PRECISION CONDITIONING UPGRADE:

Targeted busulfan intended to balance optimal engraftment with enhanced safety

Meta-analysis of 465 patients identified optimal exposure

Optimized precision dosing designed to enhance tolerability

Lowest rate of adverse events in the Bu90 range



Bu: Busulfan; AUC: Area Under the Curve
Sources: Bartelink IH et al, Lancet Haematol, 2016

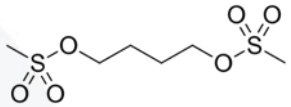
plato™ UPGRADE 2

PRECISION CONDITIONING UPGRADE:

Designed to access “hard-to-reach” compartments

BRAIN

Busulfan crosses blood-brain barrier and eliminates resident microglia cells making space for gene-modified cells



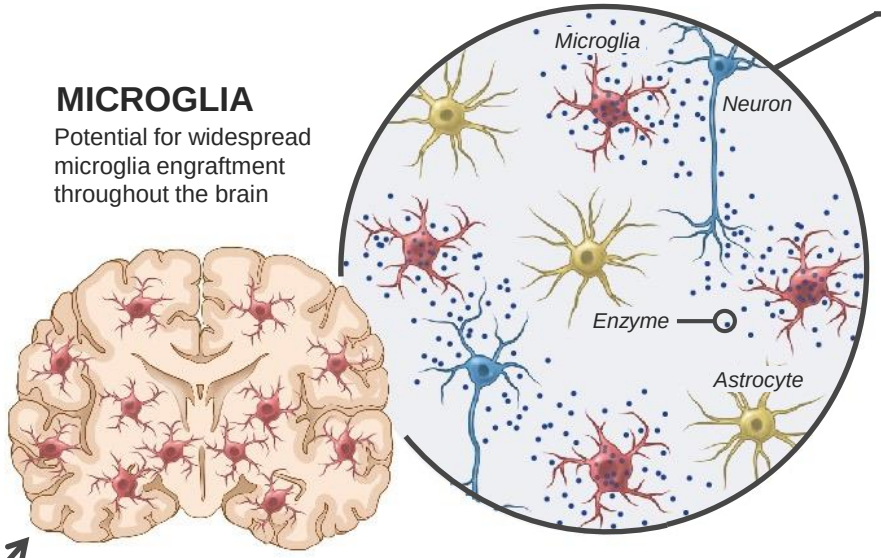
IN THE BONE MARROW

Busulfan eliminates hematopoietic (CD34+) stem and progenitor cells making space for gene-modified cells

TRANSDUCED CD34+ CELLS

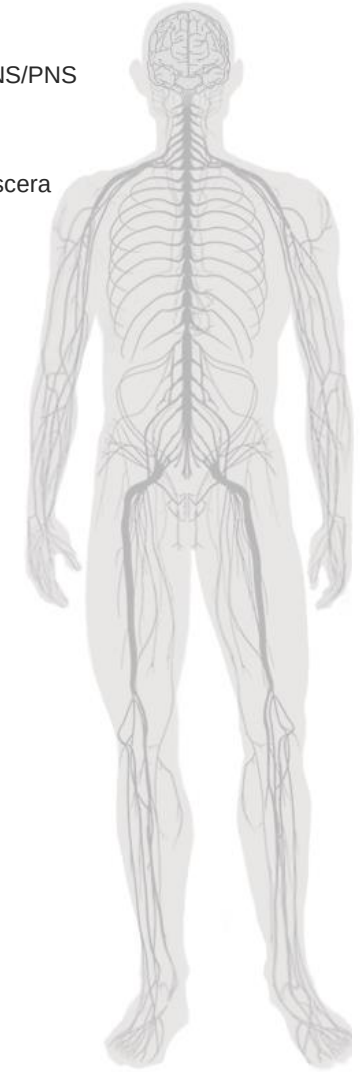
MICROGLIA

Potential for widespread microglia engraftment throughout the brain

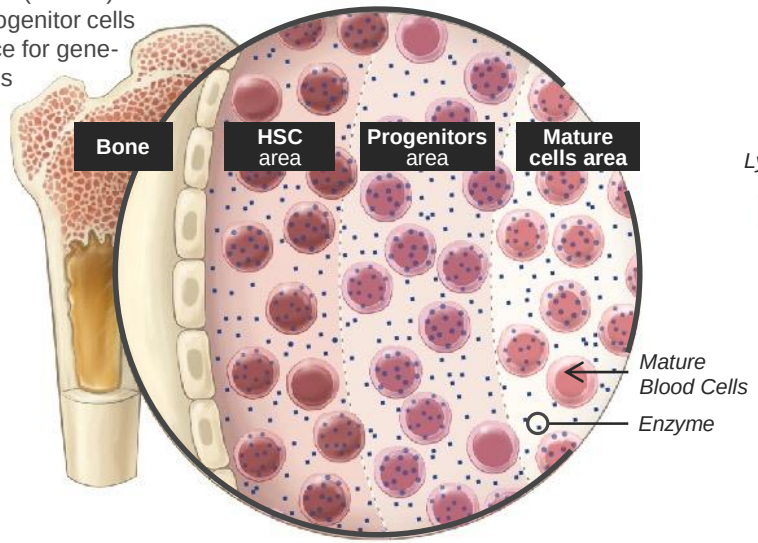


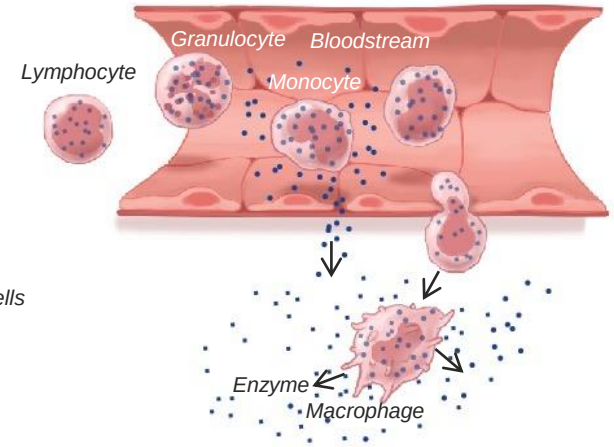
CNS/PNS

Viscera



BONE MARROW → PERIPHERAL TISSUE





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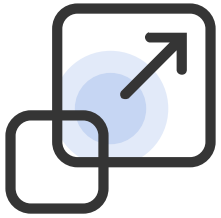
plato™ UPGRADE 3

AUTOMATION UPGRADE:

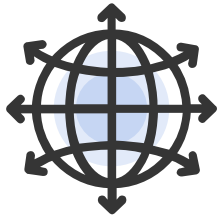
Automated, scalable manufacturing system

Designed to elevate quality and overcome historic CMC bottlenecks



Expanded Scale

Potential to reach thousands of patients per year

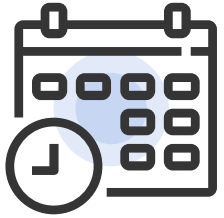


Broader Reach

Portable platform designed for flexible global production using low grade clean rooms

High Quality

Automated, closed system designed to improve quality and consistency



Enhanced Convenience

Cryopreservation simplifies logistics and patient scheduling

Lower Costs

Designed to create efficiencies in vector design / scalable cell and vector production

POWERED BY AVROBIO plato™

plato™ UPGRADE 3

AUTOMATION UPGRADE:

Poised to manufacture at scale

Designed to optimize potency and safety, and overcome historic CMC bottlenecks

VECTOR	DRUG PRODUCT
2,400 PATIENTS ANNUALLY	2,400 PATIENTS ANNUALLY
~50 patients per run	**100** patients per unit per year
~12 runs per year per suite (200 L scale bioreactor runs (10^9 titre))	**8** automated units per suite
4 production suites	**3** global production suites

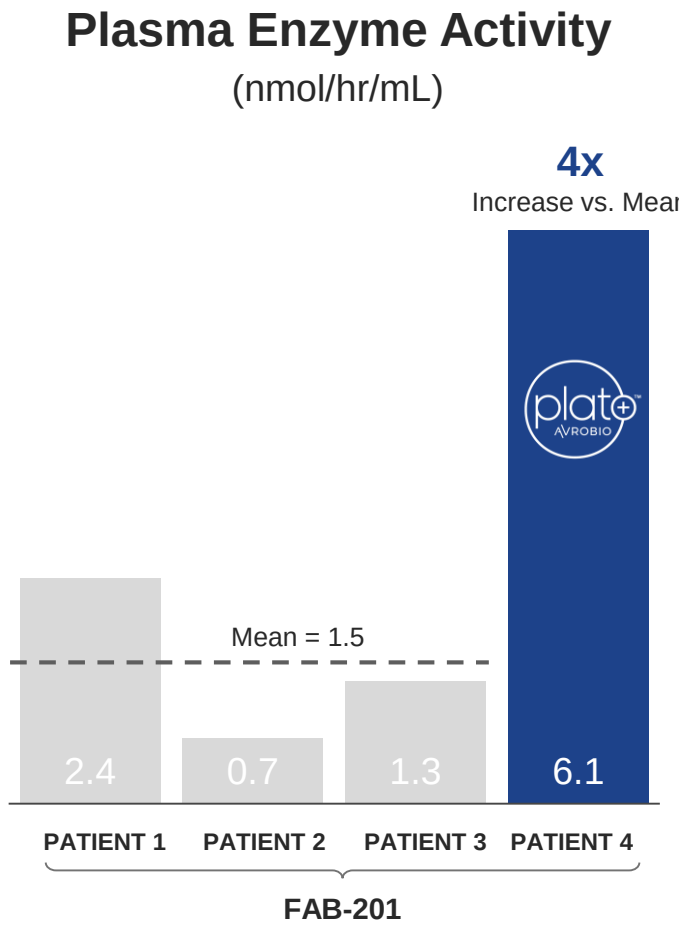
Illustrative

plato™ UPGRADE 1, 2, 3

3 UPGRADES IN PLACE:

plato™ metric compared to academic process

FAB-201 ONE MONTH data for patient #4 with plato™ vs. patients #1-3



FAB-201: AVR-RD-01 Study

Milestones anticipated across the pipeline in 2020

FABRY

- Continue recruitment in FAB-201
- Continue to report data across Phase 1 and Phase 2 trials

GAUCHER

- Dose first patient in Q2 2020
- Report initial patient data in H2 2020

CYSTINOSIS

- Continue enrollment in investigator-sponsored trial
- Continue to report patient data

POMPE

- Complete preclinical IND-enabling activities

AVROBIO to hold first R&D Day in 2020

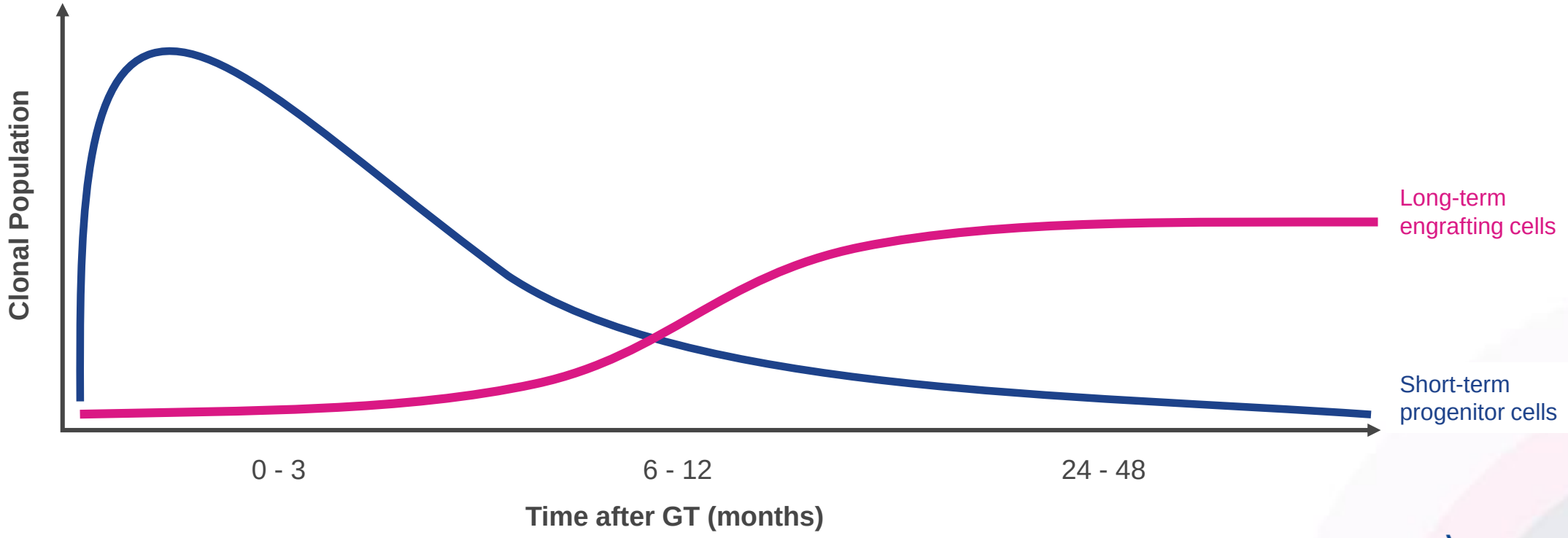
POWERED BY plato™

Appendix

Hematopoietic reconstitution occurs in two distinct phases

A few thousand long-term engrafting cells stably sustain levels of transgene product

First wave of short-term progenitor cells start to exhaust with progressive takeover by a smaller population of long-term engrafting cells



Source: Biasco L et al, Cell Stem Cell, 2016

Precedent for use of kidney biopsy data for FDA approval of drug candidate for Fabry disease

Migalastat approved on % reduction in GL-3 inclusions per KIC as compared to placebo


CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208623Orig1s000

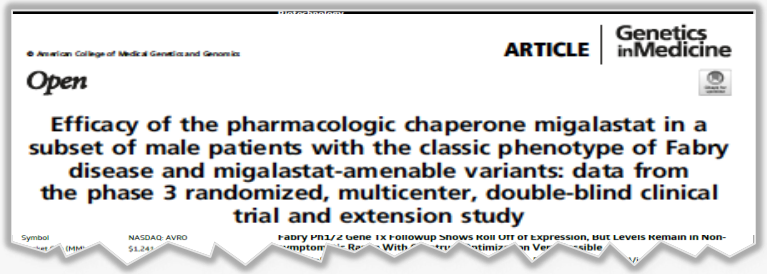
45 Amenable patients* (16 males / 29 females)

Group	Migalastat (BL –M6)	Placebo (BL –M6)
Males (N=16)	5/7 (71%) -1.10 (-1.94, -0.02)	4/9 (44%) -0.03 (-1.00, 1.69)
Patients with baseline GL-3 ≥ 0.3 (N=17; 9 males, 8 females)	7/9 (78%) -0.91 (-1.94, 0.19)	2/8 (25%) -0.02 (-1.00, 1.69)
Patients with baseline GL-3 < 0.3 (N=28; 7 males, 21 females)	6/16 (38%) -0.02 (-0.10, 0.26)	7/12 (58%) -0.05 (-0.16, 0.14)

7/9 males ≥ 50% reduction
(at 6 months from baseline)

Treatment Group	n	Baseline Median (min, max)	Month 6 Median (min, max)	Change from Baseline Median (min, max)
Average number of GL-3 inclusions per KIC (N=13)				
Galafold	7	3.6 (0.2, 6.0)	2.6 (0.1, 6.0)	-0.7 (-1.7, 1.2)
Placebo	6	1.8 (0.1, 2.8)	2.0 (0.05, 4.3)	-0.04 (-0.5, 1.5)

28% average reduction
(at 6 months from baseline)


American College of Medical Genetics and Genomics

ARTICLE | Genetics inMedicine

Open

Efficacy of the pharmacologic chaperone migalastat in a subset of male patients with the classic phenotype of Fabry disease and migalastat-amenable variants: data from the phase 3 randomized, multicenter, double-blind clinical trial and extension study

Source: *Germain D et al, Genetics in Medicine, 2019*

Classic Fabry patient level data

0-6 months randomized clinical trial and 6-12 months open label extension

	Male Patients with the Classic Phenotype													
	Migalastat (Months 0-24)							Placebo (Months 0-6) → Migalastat (Months 6-24)						
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14
PTC GL-3 inclusions at BL	0.16	0.03	n/a	5.69	1.22	n/a	2.88	2.41	1.55	0.16	0.03	0.11	0.94	0.88
Change in PTC GL-3 inclusions from BL to M6	-0.08	0.01	n/a	-1.77	-1.10	n/a	-1.25	1.21	-0.21	0.01	0.09	-0.07	1.94	-0.83
Change in PTC GL-3 inclusions from BL/M6[b] to M12	-0.12	n/a	n/a	-1.92	n/a	n/a	-0.81	-0.94	-1.13	-0.09	-0.05	n/a	-2.28	0.06

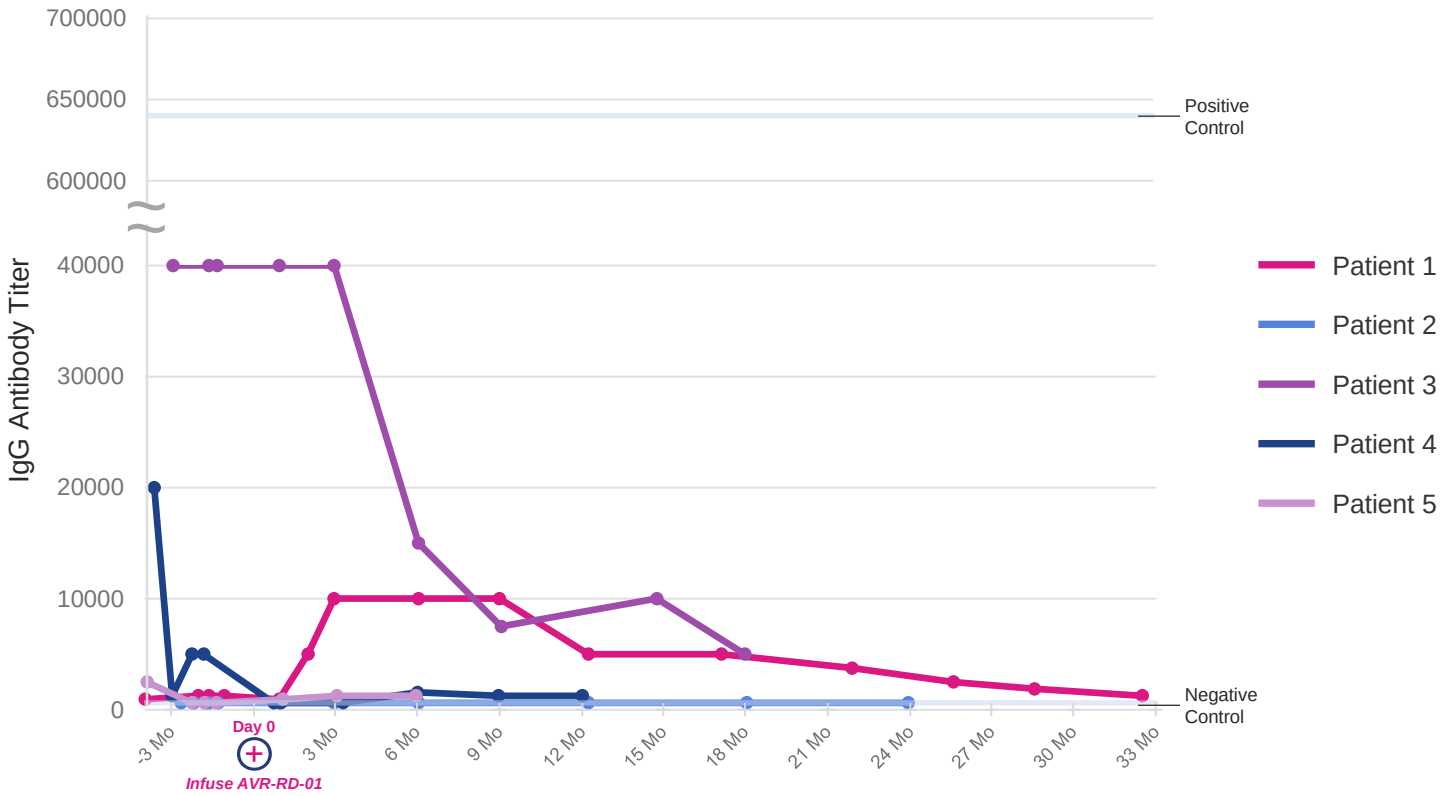
46% average reduction
(average of patients with 12 month data)

- *Classic Fabry disease (AGA activity <1%)*
- ***NOTE:** For informational purposes; differences exist between trial designs and subject populations; AVROBIO has not conducted any head-to-head trials comparing migalastat to AVR-RD-01*

Reduction of pre-existing anti-ERT drug IgG antibodies following AVR-RD-01

Suggests potential as a therapeutic option independent of pre-existing antibodies

Fabry Disease Phase 1 IgG Antibody Titer



Similar Results Observed in Other Studies

San Raffaele Telethon Institute for Gene Therapy (SR-TIGET)

Change in pre-existing antibodies reported for Hurler disease (MPS-1)

- Ex vivo LV-CD34+ gene therapy with conditioning
- N = 6
- Evaluable patients (5/6) demonstrated sustained, supraphysiologic blood IDUA activity
- 4/5 prior ERT (rhIDUA) exposure (5-28 months)
- 4/5 pre-existing ERT-induced IgG antibodies
- 6/6 anti-rhIDUA IgGs undetectable 2 months post gene therapy

Source: *Gentner B et al., Blood, 2019*

ERT: Enzyme Replacement Therapy; IgG: Immunoglobulin G; MPS-1: Mucopolysaccharidosis Type 1; IDUA: Iduronidase: SR-TIGET: San Raffaele Telethon Institute for Gene Therapy; LV: Lentiviral; rhIDUA: Recombinant Human alpha-L-Iduronidase